UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/786,725	04/23/2001	Hans-Werner Heinrich	101195-44	4120

27387 7590 09/02/2009

NORRIS, MCLAUGHLIN & MARCUS, P.A.
875 THIRD AVE
18TH FLOOR
NEW YORK, NY 10022

EXAMINER	
WILLIAMS, KAREN M	
ART UNIT	PAPER NUMBER
PCT	
MAIL DATE	DELIVERY MODE
09/02/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/786,725	HEINRICH ET AL.	
	Examiner	Art Unit	
	JAMES L. GRUN	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 May 2008, 10 July 2008, & 19 May 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-15 and 17-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-15 and 17-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

The amendments filed 27 May 2008 (entered in part), 10 July 2008 (bona fide, not fully responsive), and 19 May 2009 are acknowledged. Claims 1, 3-15, 17-22 remain in the case.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention, and failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

Claims 1, 3-11 and 17-22 are rejected under 35 U.S.C. 112, first paragraph, for reasons of record, that the specification contains subject matter which was not described in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, and which was not described in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. For the reasons of record, the issue is whether the disclosure describes and supports the ability of the recited peptides to elicit antibodies that bind singly, or in combination, and function for determination of all elastase isoforms in a body fluid sample.

As set forth previously, applicant teaches only polyclonal antibodies to particular peptides and provides no description or guidance to any single antibody or monospecific species which functions in the invention to bind to all known elastase iso-enzymes. The exemplified

antibodies bind to the peptides used as immunogens or to elastase in a Western blot after sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE). Applicant states that "not every antibody detects all isoforms" in this assay (see page 10), appearing to imply that some antibodies (or combinations?) bind all isoforms. However, there is nothing in the specification to indicate which, if any, of the anti-peptide antibodies bind to all isoforms so that one could practice the invention as desired and claimed to detect all isoforms with a single antibody absent further unguided unpredictable experimentation to complete applicant's suggested invention. As set forth, adequate written description requires more than a mere statement that a product is part of the invention, more than a reference to a potential method of isolating it, and more than a generic statement which defines a genus of products by only their functional activity. As set forth, the product itself is required as well as recitation of a representative number of products falling within the scope of a claimed genus. Moreover, as set forth, all possible analogs of a product are not enabled by a disclosure wherein the characteristics of the analogs are unpredictable. As set forth, a patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. As set forth, absent further written description and guidance from applicant, one would have no assurance of successfully obtaining appropriate functional reagents and predictably performing the method as suggested by applicant. For the reasons of record, and as summarized above, applicant has not described or enabled any antibody which functions **singly** as claimed.

For reasons of record, applicant also provides no guidance for usable combinations. In this regard, as set forth, some of the peptides suggested for use by applicant would be expected to elicit antibodies that bind to an isoform which corresponds to porcine elastase, which is not

expressed in the human pancreas (see e.g. Tani et al., page 1231, and Fig. 9), and which would complicate the assay in certain patient populations, such as those patients receiving enzyme replacement therapy with animal, such as porcine, pancreatic enzymes (see Schneider et al. in this regard). Moreover, as set forth, one would not be able to perform a sandwich assay with combinations that do not bind to epitopes found at two sites on the same enzyme molecule, e.g. a combination would not function in the invention in which one antibody binds elastase I as known to the art (i.e. elastases IIIA and/or IIIB, see e.g. Tani et al.) and the other binds to an epitope on the un-expressed isoform (i.e. elastase I, see e.g. Tani et al.) which does not cross-react with elastase I (i.e. elastases IIIA and IIIB, see e.g. Tani et al.), combinations suggested by applicant's disclosure.

Moreover, the abstract of Weiss et al. teaches that applicant was not in possession of the invention as claimed in 2006 because antibodies produced by the instant assignee (BIOSERV) and used in assays of stool elastase are clearly shown not to bind all isoforms of elastase. Further experimentation is taught as required by the reference for one to assess the specific differences and prognostic value of elastase isoforms in the assessment of exocrine pancreatic insufficiency. These results contrast with the results of Schneider et al. in which previous antibodies produced by the instant assignee (BIOSERV) and used in assays of stool elastase in 2005 are suggested to bind to porcine enzymes. Again, functional combinations are not clearly disclosed by applicant so that one would know without question what combinations predictably functioned in applicant's suggested invention when the application was originally filed.

As set forth previously, applicant teaches only polyclonal antibodies to particular peptides and provides no description or guidance to any antibodies or combination of antibodies

capable of predictable binding to any or all of the elastase enzyme isoforms as found in stool or body fluid samples, because only binding to proteins in Western blots, i.e. after SDS denaturation, is specifically exemplified. One could not predict the ability of any of the antibodies to the suggested peptides to bind to non-denatured protein as found in a fluid sample from a patient. As set forth, adequate written description requires more than a mere statement that a product is part of the invention, more than a reference to a potential method of isolating it, and more than a generic statement which defines a genus of products by only their functional activity. As set forth, the product itself is required as well as recitation of a representative number of products falling within the scope of a claimed genus. Moreover, as set forth, all possible analogs of a product are not enabled by a disclosure wherein the characteristics of the analogs are unpredictable. As set forth, a patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. As set forth, absent further written description and guidance from applicant, one would have no assurance of successfully obtaining appropriate functional antibody reagents and predictably performing the method as suggested by applicant.

Applicant's arguments filed 27 May 2008 have been fully considered but they are not deemed to be persuasive.

Applicant urges that a specific combination of antibodies that would function in the invention would be apparent to one skilled in the art. This is not found persuasive for the extensive reasons of record and because, as set forth, "there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is

within the skill of the art", "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement."

Applicant urges that the antibodies of the invention are specific. This is not found persuasive because the argument is not supported by any evidence of record commensurate in scope with the invention as claimed. In this regard the results of Schneider et al., in which previous antibodies produced by the instant assignee (BIOSERV) and used in assays of stool elastase in 2005 are suggested to bind to porcine enzymes, are again noted by the examiner. Applicant has previously urged that such cross-reactivity can be eliminated by elimination of an antibody from the combination as taught in the abstract of Weiss et al. This was not found persuasive because the argument is not consistent with or commensurate in scope with the invention as disclosed and claimed and does not inform one as to which, if not all, embodiment(s) of applicant's suggested and claimed method is(are) inoperative.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3-6, and 18-21 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 3-5, 20, and 21 involve method claims and, as such, they should clearly set forth the various method steps in a positive, sequential manner using active tense verbs such as mixing, reacting, and detecting. "Employing" or "using" or similar terms are not valid method steps. In claim 4, "the antigen" lacks antecedent basis.

In claim 3 and claims dependent thereupon, it is not clear how antibodies are obtained "by means of antigens," e.g. it is not clear what applicant intends as encompassed because it is not clear if the antigens are immunogens, or binders in affinity chromatography, or used in some other means.

In claim 6, "the pancreas" lacks antecedent basis.

Claim 18 is indefinite in that the claims fail to further limit the subject matter of a previous claim and set forth an intended use but fail to point out what components are included or excluded by the claim language.

In claim 19, the interrelationships of the components are not clear, e.g. it is not clear if hemocyanin is a carrier substance.

In claim 20, the interrelationships of the components are not clear, e.g. it is not clear if peptides are sub-units. It is not clear what is intended by "myeoloma cells" or "hybridoma cells which are cultivated in cell lines."

Applicant's arguments filed 27 May 2008 have been fully considered but they are not deemed to be persuasive.

Notwithstanding applicant's assertions to the contrary, the rejected claims remain unclear for the reasons of record and as set forth above. Although claims are interpreted in light of the disclosure, limitations from the specification are not read into the claims unnecessarily. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). See also *In re Zletz*, 893 F.2d 319, 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989) ("During patent examination the pending claims must be interpreted as broadly as their terms reasonably allow.... The reason is simply that during patent prosecution when claims can be amended, ambiguities should be recognized, scope

and breadth of language explored, and clarification imposed.... An essential purpose of patent examination is to fashion claims that are precise, clear, correct, and unambiguous. Only in this way can uncertainties of claim scope be removed, as much as possible, during the administrative process.").

Notwithstanding applicant's assertions to the contrary, applicant's amendments have not obviated rejections under this statute for the reasons set forth above.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-8, 10-15, and 17-22 are rejected under 35 U.S.C. § 102(b) as being anticipated by Scheefers et al. (US 5,622,837) in light of the instant disclosure for reasons of record.

Claims 1, 3-8, 10, 12-15, 17, 18, 21, and 22 are rejected under 35 U.S.C. § 102(b) as being anticipated by Sziegoleit et al. (Clin. Biochem. 22: 79, 1989) in light of the instant disclosure for reasons of record.

Applicant's arguments filed 27 May 2008 have been fully considered but they are not deemed to be persuasive.

In contrast to previous arguments, applicant now urges that the antibodies of the prior art are specific for many different epitopes of elastases IIIA and IIIB, bind other enzymes, and are not appropriate for diagnosis. These are not found persuasive for the reasons of record and

because applicant has provided no *factual* evidence of a difference for the reagents as instantly claimed and those as used in the references. As set forth, Sziegoleit et al. teach elicitation of polyclonal antibodies to purified enzyme and Scheefers et al. teach elicitation of both polyclonal and monoclonal antibodies to purified enzyme and fragments thereof, not only to the suggested antigen/immunogen as instantly excluded, for use in sandwich enzyme-linked immunosorbent assay for diagnosis of pancreatic diseases. As set forth, the enzyme preparation would inherently be a mixture of at least the elastase I isoforms (i.e. elastases IIIA and IIIB), comprising the peptides as instantly claimed, and polyclonal antibodies elicited thereto would inherently bind to the isoforms and cross-react with similar epitopes as found in elastase II. Moreover, the teaching of a preferred peptide does not serve to teach away from any other fragment of the enzyme as taught for use in Scheefers et al. (see e.g. col. 2). As set forth, the Patent and Trademark Office does not have the facilities and resources to provide the *factual* evidence needed in order to establish that there is a difference, in the first place, between the reagents of the prior art and those instantly disclosed and, that if there is such a difference, that such a difference would have been considered unexpected, i.e. unobvious, by one of ordinary skill in the art. The burden is upon applicant to present such factual evidence. See e.g. In re Best (195 USPQ 430 (CCPA 1977)) or Ex parte Phillips (28 USPQ2d 1302 (BPAI 1993)). Applicant's arguments have not met this burden.

Applicant urges that the claimed invention is already practically used as evidenced by the abstract of Weiss et al. (published variously in: J. Ped. Gastroenterol. Nut.; Pancreatology; and Pancreas). This is not found persuasive because the showing in the abstract of Weiss et al. teaches that applicant was not in possession of the invention as claimed because antibodies

produced by the instant assignee (BIOSERV) and used in assays of stool elastase are clearly shown not to bind all isoforms of elastase.

The art made of record and not relied upon is considered pertinent to applicant's disclosure.

Tani et al. (J. Biol. Chem. 263: 1231, 1988) teach the sequences of human elastase genes (see Fig. 9). The reference teaches that the sequence identified therein as elastase I is not expressed in human adult pancreas (see page 1231, col. 2) and that the sequences identified therein as elastase III are human elastase I as known to the art (see page 1237, col. 2).

Geokas et al. (J. Biol. Chem. 252: 61, 1977) teach an immunoassay for human elastase II in human serum and the elevation of the enzyme therein in individuals with acute pancreatic inflammation (see paged 66, col. 2).

Schneider et al. (Clin. Chem. 51: 1052, 2005) teach complications if antibodies in a human elastase detection assay bind to porcine elastases.

The abstract of Weiss et al. (published variously in: J. Ped. Gastroenterol. Nut.; Pancreatology; and Pancreas) teaches that applicant was not in possession of the invention as claimed in 2006 because antibodies produced by the instant assignee (BIOSERV) and used in assays of stool elastase are clearly shown not to bind all isoforms of elastase. Further experimentation is taught as required by the reference for one to assess the specific differences and prognostic value of elastase isoforms in the assessment of exocrine pancreatic insufficiency.

Harlow et al. teach that, once the amino acid and/or nucleic acid sequences of a protein are known, it is routine and conventional in the art to elicit antibodies to peptides and/or fusion

proteins derived from the protein and/or to prepare a bank of site-specific monoclonal antibodies for use (pages 72-77). Harlow et al. teach rationales for the selection of synthetic peptides as immunogens and suggest the carboxyl-terminal or amino-terminal peptide sequences or internal hydrophilic regions as desirable starting peptide immunogens (page 76).

Stein et al. (Clin. Chem. 42: 222, 1996) teach the clinical evaluation of the fecal elastase assay of Scheefers et al. (US 5,622,837).

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR REPLY TO THIS FINAL ACTION IS SET TO EXPIRE **THREE MONTHS** FROM THE MAILING DATE OF THIS ACTION. IN THE EVENT A FIRST REPLY IS FILED WITHIN **TWO MONTHS** OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE **THREE-MONTH** SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR REPLY EXPIRE LATER THAN **SIX MONTHS** FROM THE MAILING DATE OF THIS FINAL ACTION.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James L. Grun, Ph.D., whose telephone number is (571) 272-0821. The examiner can normally be reached on weekdays from 11 a.m. to 7 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya, SPE, can be contacted at (571) 272-0806.

The phone number for official facsimile transmitted communications to TC 1600, Group 1640, is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application, or requests to supply missing elements from Office communications, should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/J. L. G./
James L. Grun, Ph.D.
Examiner, Art Unit 1641
September 1, 2009

/Ann Y. Lam/
Primary Examiner, Art Unit 1641
August 30, 2009